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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

May 1, 1998

MEMORANDUM

SUBJECT: Pirimiphos-methyl (List B Case No. 2535/Chemical ID No. 108102). Guideline Nos. 860.1480/860.1380/860.1340. Magnitude of the Residue in Meat, Milk, Poultry and Eggs, Including Analytical Methods and Storage Stability Data.

MRID Nos. 440464-01 through -04; 44055001, 44059901, and 00080777.

DP Barcode Nos. D194803 and D228209.

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THROUGH: Whang Phang, Ph.D., Branch Senior Scientist
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Please find attached a review of the ruminant and poultry feeding studies (and associated analytical methods and storage stability data) submitted by Wilbur-Ellis in support of reregistration of products containing the active ingredient pirimiphos-methyl. The data were reviewed by Dynamac under supervision of HED, and have been revised to reflect current Agency policies.

In a meeting held 4/16/98, the HED Metabolism Assessment Review Committee (MARC) determined that the tolerance expression for pirimiphos-methyl [40 CFR §180.409] should be revised to include residues of the parent only. For the purpose of risk assessment, the des-ethyl metabolite (R36341) will be included in the total toxic residue; hydroxy-pyrimidine metabolites currently included in the tolerance expression will be deleted from the tolerance expression, and will not be considered in risk assessment. Based on this conclusion, and on the submitted ruminant and poultry feeding studies, HED concludes the following:

The ruminant and poultry feeding studies are adequate for the purpose of reregistration and tolerance reassessment; the data indicate that tolerances for residues in meat (of cattle, goat, hogs, horses and sheep), milk, eggs, poultry meat and poultry meat by-products can be classified under category 3 of 40 CFR §180.6(a), i.e. there is no reasonable expectation of detectable residues. Therefore, tolerances for residues in these commodities are not necessary, and should be revoked. Tolerances for residues in the fat and meat by-products of cattle, goats, hogs, horses and sheep and in poultry fat should be revised to 0.02 ppm; separate tolerances for residues in liver and kidney of cattle, goats, hogs, horses and sheep should be revoked.

Note: these conclusions could change if additional uses of pirimiphos-methyl result in calculation of a higher theoretical dietary burden, or if direct dermal application is proposed.

cc: CSwartz; List B Rereg. File; SF.
CSwartz:RRB1:CM2:Rm804F:703 305 5877:04/23/98
Secondary Review:C.L. Olinger:04/30/98 RRB1 ExpoTeam Review:04/30/98

PIRIMIPHOS-METHYL

Shaughnessy No. 108102; Case 2535

(CBRS Nos. 12504 and 17420; DP Barcodes D194803 and D228209)

Registrant's Response to Residue Chemistry Data Requirements

March 27, 1997

Contract No. 68-D4-0010

Submitted to:
U.S. Environmental Protection Agency
Arlington, VA

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PIRIMIPHOS-METHYL

Shaughnessy No. 108102; Case 2535

(CBRS Nos. 12504, 17420; DP Barcodes D194803, D228209)

REGISTRANT'S RESPONSE TO RESIDUE CHEMISTRY DATA REQUIREMENTS

BACKGROUND

The pirimiphos-methyl Phase IV Review (1/91) required residue studies depicting the magnitude of pirimiphos-methyl and regulated metabolites in milk and eggs, and in tissues of dairy cattle and poultry fed pirimiphos-methyl at 1x, 3x, and 10x the maximum theoretical dietary burden. Method validation studies were required for analytical methods used to determine residues of pirimiphos-methyl and the des-ethyl metabolite [R36341] in livestock samples. In addition, storage stability data were required to be submitted in support of all residue studies. In response, Compliance Services International, on behalf of the Wilbur-Ellis Company, has submitted the following data: magnitude of the residue studies in cattle and poultry (1996; MRIDs 44059901 and 44046402), supporting storage stability data (1996; MRIDs 44046404 and 44046403), and validation data for livestock analytical methods (1996; MRIDs 44046401 and 44055001). The original analytical method was included in the submission (MRID 00080777), as well as data pertaining to analytical standards (1996; MRID 44057701). These data are reviewed herein for adequacy in fulfilling outstanding residue chemistry data requirements.

Tolerances are established (40 CFR §180.409) for residues of pirimiphos-methyl and its metabolite O-[2-ethylamino-6-methyl-pyrimidin-4-yl) O,O-dimethyl phosphorothioate [R36341] and, in free and conjugated form, the metabolites 2-diethylamino-6-methyl-pyrimidin-4-ol, 2-ethylamino-6-methyl-pyrimidin-4-ol, and 2-amino-6-methyl-pyrimidin-4-ol in corn (8.0 ppm); sorghum grain (8.0 ppm); kiwifruit (5.0 ppm); eggs (0.5 ppm); milk fat [3.0 ppm; 0.1 (N) in whole milk]; fat of cattle, goats, hogs, horses, poultry, and sheep at 0.2 ppm; kidney and liver of cattle, goats, hogs, horses, and sheep at 2.0 ppm; meat and meat byproducts of cattle, goats, hogs, horses, and sheep at 0.2 ppm; and meat and meat byproducts of poultry at 2.0 ppm. Food and feed additive tolerances have been established in 40 CFR §185.4950 and §186.4950 for residues in corn milling fractions (except flour) and in sorghum milling fractions (except flour) at 40 ppm and in 40 CFR §185.4950 for residues in corn oil at 88 ppm. The tolerances for residues in corn and sorghum grain were established in conjunction with registration of products containing the active ingredient pirimiphos-methyl for postharvest application to stored grain.

In a meeting held 4/16/98, the HED Metabolism Assessment Review Committee (MARC) discussed the residues to be regulated under 40 CFR §180.409 (refer to the J. Stokes memo dated 4/13/98). In order to harmonize with CODEX, the only residue which will be included

in the tolerance expression is the parent, pirimiphos-methyl. The des-ethyl metabolite, which is considered to be of toxicological concern, will not be included in the tolerance expression, but will be included in the Agency's dietary risk assessments. The hydroxy-pyrimidine metabolites will no longer be included in the tolerance expression or in Agency risk assessments. Although the studies reviewed herein include data pertaining to the hydroxy-pyrimidine metabolites, these data are not discussed since the metabolites are to be removed from the tolerance expression.

CONCLUSIONS

1. In a ruminant feeding study, lactating dairy cows were dosed with pirimiphos-methyl for 27 days at 40, 120, and 400 ppm in the diet, representing 4X, 12X and 40X the maximum theoretical dietary burden of 10 ppm. Milk was collected twice daily, and additional milk samples were separated into cream and skim milk. Cows were sacrificed within 24 hours of the last dose, and subcutaneous fat, peritoneal fat, skeletal muscle, liver and kidneys were collected. All samples were stored at -20 C prior to analysis within 51 days of sample collection.

2. In a poultry feeding study, hens were dosed with pirimiphos-methyl for 28 days at 47 and 141 ppm in the diet, representing 8X and 24X the maximum theoretical dietary burden of 6.4 ppm. A dose level of 523 ppm (82X) was attempted, but it was not tolerated by the hens. Eggs were collected twice daily. Within 24 hours of the last dose, hens were sacrificed and breast and thigh muscle, liver, abdominal fat, and skin with subcutaneous fat were collected. Samples were stored at -20 C prior to analysis within 6 months of sample collection.

3. Samples from the poultry and ruminant feeding studies were analyzed for residues of pirimiphos-methyl and its metabolite R36341 following extraction and subsequent quantitation using gas chromatography with flame photometric detection (GC/FPD). Adequate method validation data have been submitted for the method, which is a modification of the ICI Method 11A. The method is essentially the same as Method I in PAM, Vol.II. Adequate concurrent method recoveries were achieved during analysis of feeding study samples.

4. A 6-month storage stability study was conducted, and demonstrated stability of pirimiphos-methyl *per se* and metabolite R36341 in all livestock matrices stored frozen for up to 6 months. These data are adequate to support the submitted feeding studies.

5. The ruminant and poultry feeding studies are adequate for the purpose of reregistration and tolerance reassessment, and are supported by adequate analytical methods and storage stability data.

6. Based on data from the ruminant feeding study, and on the inclusion of only the parent, pirimiphos-methyl, in the tolerance expression, tolerances for residues in meat (of cattle, goats, hogs, horses and sheep) and milk can be classified under category 3 of 40 CFR §180.6(a), i.e. there is no reasonable expectation of detectable residues. Therefore, tolerances for residues in meat and milk are not necessary, and should be revoked. Tolerances for residues in the fat and meat by-products of cattle, goats, hogs, horses and sheep should be revised (decreased) to 0.02 ppm. Separate tolerances for residues in liver and kidney of cattle, goats, hogs, horses and sheep should be revoked.

7. With the revision of the tolerance definition to include only the parent compound, data from the poultry feeding study indicate that tolerances for residues in eggs, poultry meat and meat by-products can be classified under category 3 of 40 CFR §180.6(a). Therefore, tolerances for residues in eggs, and in poultry meat and meat by-products should be revoked. The tolerance for residues in poultry fat should be revised (decreased) to 0.02 ppm.

DETAILED CONSIDERATIONS

Ruminant and Poultry Feeding Studies (MRIDs 44059901 and 44059902)

Livestock feed items with established tolerances for pirimiphos-methyl residues include corn grain, sorghum grain, and milled fractions of corn and sorghum grain (except flour). Recent residue studies and processing studies on corn and sorghum indicated the following: (i) tolerances for residues in corn and sorghum grain should remain at 8 ppm; (ii) based on the average concentration factor for aspirated grain fractions and the highest average field trial (HAFT) residue in corn, a tolerance of 20 ppm is required for residues in aspirated grain fractions; and (iii) the tolerances for residues in milled fractions of corn and sorghum should be revoked since no concentration was observed in corn milled fractions and since the Agency no longer establishes tolerances for residues in sorghum milled fractions.

The maximum theoretical dietary burden is 10 ppm for cattle based on a diet consisting of 60% corn grain (revised tolerance of 8 ppm, adjusted for 85% DM) and 20% aspirated grain fractions (20 ppm tolerance needed, adjusted for 85% dry matter). The maximum theoretical dietary burden is 6.4 ppm for poultry, based on a diet consisting of 80% corn grain (no adjustment for dry matter content necessary).

Ruminants

Groups of 3 cows were dosed orally with pirimiphos-methyl at nominal daily rates equivalent to 40, 120, or 400 ppm in the diet for 27 days. These dose levels represent 4X, 12X and 40X the maximum theoretical dietary intake of pirimiphos-methyl for beef cattle. A fourth group served as controls. Milk was collected twice daily. On days 14 and 27 additional milk

samples were taken and separated into cream and skim milk. Within 24 hours of the last dose, the animals were sacrificed, and subcutaneous fat, peritoneal fat, skeletal muscle, liver and kidneys were collected. All samples were stored at -20 C. Analyses were conducted within 51 days of sample collection.

Poultry

Groups of 12 hens were dosed orally with pirimiphos-methyl at actual daily rates of 52 or 157 ppm in the diet for 28 days. A third group was dosed at 523 ppm, but the dosing was discontinued after 17 days because the birds showed adverse effects. These dose levels represent 8X, 24X and 82X the maximum theoretical dietary intake of pirimiphos-methyl for poultry. A fourth group served as controls. Eggs were collected twice daily and pooled into three or four subgroups within each dose group. Within 24 hours of the last dose, the hens were sacrificed and breast and thigh muscle, liver, abdominal fat, and skin with subcutaneous fat were collected. Tissues were pooled into three or four subgroups within each dose group. All samples were stored at -20 C. Analyses were conducted at Huntingdon Life Sciences, Ltd. within 6 months of sample collection.

Residue Analytical Methods (MRIDs 44055001 and 44046401)

Validation data were submitted for modifications of the original ICI Method 11A for pirimiphos-methyl and its phosphorous containing metabolites in cattle and chickens; these submissions also contained validation data for methods to quantify the hydroxy-pyrimidine metabolites R46382, R35510, and R4039 [these metabolites will no longer be included in the tolerance expression, or included in Agency risk assessments]. The original method 11A (MRID 00080777) was comprised of gas chromatography (GC) methods for crops, milk, and livestock tissues, and is essentially the same as Method I in PAM, Vol.II.

The methods used to collect residue data on livestock tissues and for which validation data were submitted are described below. Validation data are summarized in Tables 1 and 2. Recoveries obtained concurrently with the residue data from livestock feeding studies are presented in Tables 3 and 4. Method validation and residue analyses were conducted at Huntingdon Research Centre, Ltd., Cambridgeshire, England.

Briefly, residues of pirimiphos-methyl and the des-ethyl metabolite (R36341) are extracted from milk with acetone:acetonitrile (50:100, v:v), and the mixture is centrifuged. The supernatant is reduced in volume and the residues are partitioned into toluene. The resulting toluene fraction is dried over sodium sulfate and evaporated to near dryness. The residues are reconstituted in a small amount of toluene and analyzed using gas chromatography with flame photometric detection in the phosphorous mode (GC/FPD). The limits of quantitation (LOQs) were 0.01 ppm for both pirimiphos-methyl and R36341.

Pirimiphos-methyl and R36341 are extracted from eggs with acetone and acetonitrile. The extract is reduced in volume and partitioned with toluene after addition of NaCl. The toluene extract is evaporated to dryness and the residues taken up in acetonitrile for analysis using GC/FPD. The LOQ for each analyte was 0.02 ppm.

Pirimiphos-methyl and R36341 are extracted from cream and tissues with acetonitrile and hexane. The acetonitrile phase is dried on sodium sulfate, reduced to near dryness, and reconstituted in acetonitrile for quantitation via GC/FPD. The LOQ for each analyte was 0.01 ppm in cream and 0.02 ppm in tissues, with the exception of cow muscle (0.05 ppm).

Recoveries from cattle tissues/milk were generally adequate, with the exception of low recoveries of pirimiphos-methyl (i.e. <70%) from whole milk and cream fortified at 0.10 ppm. In addition, a high recovery was obtained (i.e. >120%) from kidney fortified with the parent at 0.02 ppm. In poultry, high recoveries were obtained from muscle fortified with R36341 at 0.02 and 0.2 ppm, and from fat fortified at 0.2 ppm. However, concurrent recoveries were generally acceptable, and therefore HED concludes that the submitted validation data indicate the methods are sufficient for data collection for livestock commodities.

Table 1. Recovery of Pirimiphos-Methyl and R36341 from Cattle Tissues/Milk.

Matrix	Fortification (ppm)	Mean Recovery (%) [a]	
		Pirimiphos-methyl	R36341
Whole milk	0.01	92.9	89.6
	0.10	69.9	78.7
	1.00	71.7	81.9
Cream	0.01	92.4	107
	0.10	67.6	82.8
	1.00	84.6	89.3
Fat	0.02	106.5	106.5
	0.20	98.4	108.5
	2.00	89.8	99.6
Muscle	0.05	111	100.5
	0.50	89.1	109
	5.00	113	119
Liver	0.02	92.5	74.4
	0.20	92.4	89.9
	2.00	85.8	92.3

Table 1. Recovery of Pirimiphos-Methyl and R36341 from Cattle Tissues/Milk.

Matrix	Fortification (ppm)	Mean Recovery (%) [a]	
		Pirimiphos-methyl	R36341
Kidney	0.02	123	117
	0.20	108	114.5
	2.00	93.2	102.7

[a] Each value is the mean of 2-3 samples.

Table 2. Recovery of Pirimiphos-Methyl and R36341 from Hen Tissues/Eggs.

Matrix	Fortification (ppm)	Mean Recovery (%) [a]	
		Pirimiphos-methyl	R36341
Eggs	0.02	82.5	85.2
	0.20	77.4	81.2
	2.00	79.2	76.5
Muscle	0.02	100.1	126.5
	0.20	97.2	124
	2.00	89.6	107.5
Liver	0.02	96.3	92.0.
	0.20	96.9	91.6
	2.00	92.9	90.6
Fat	0.02	94.7	94.7
	0.20	98.3	120
	2.00	92.9	115
Skin/fat	0.020	97.6	90.3
	0.200	94.2	111.5
	2.00	84.9	100.5

[a] Each value is the mean of 2-5 samples.

Table 3. Concurrent Recovery of Pirimiphos-Methyl and R36341 from Cattle Tissues/Milk.

Matrix	Fortification (ppm)	Recovery (%)	
		Pirimiphos-methyl	R36341
Whole milk	0.01	78.7-107 n=7	74.4-110 n=7
	0.02	102	87.3
	0.10	82.8-99.6 n=6	88.3-106 n=6
	1.0	88.0, 74.1 n=2	90.1, 81.2 n=2
Cream	0.01	89.2, 71.7	
	0.10	75.4, 70.9	64.7, 98.1
Liver (cow)	0.02	118	
	2.00	104	115
Kidney (cow)	0.02	106	77.5
	2.00	79.5	76.6
Muscle (cow)	0.05	101	93.8
	2.00	116	112
Fat and skin/fat	0.02	107, 118	110, 108
	0.20	98.0, 107	109, 109

Table 4. Concurrent Recovery of Pirimiphos-Methyl and R36341 from Hen Tissues/Eggs.

Matrix	Fortification (ppm)	Recovery (%)	
		Pirimiphos-methyl	R36341
Eggs	0.02	75.6-100 n=8	67.4-84.1 n=8
	0.20	64.0-99.6 n=8	57.2-89.9 n=8
Liver (hen)	0.02	112	72.2
	0.20	99.1	98.8
Muscle (hen)	0.02	115	98.7
	0.20	108	111
Fat and skin/fat	0.02	99.6, 107	97.5, 110
	0.20	110, 120	116, 125

Results

Ruminants

Refer to the residue levels summarized in Tables 5 and 6. At the lowest dose level of 40 ppm (4X) pirimiphos-methyl and R36341 residues were nondetectable (<0.01 ppm) in milk and cream throughout the 27-day study. At 12X, pirimiphos-methyl and R36341 residues were nondetectable (<0.01 ppm) in milk; at 12X, pirimiphos-methyl residues in cream were 0.044 ppm and 0.028 ppm on study days 14 and 27, respectively. In cream from cows dosed at 12X, R36341 residues were 0.059 and 0.026 ppm on study days 14 and 27, respectively.

At 40X, mean pirimiphos-methyl residues in milk increased to a maximum of 0.034 ppm on day 5 (the maximum single sample residues was 0.052 ppm), and decreased to nondetectable (<0.01 ppm) levels by study day 24. At 40X, mean metabolite R36341 residues increased to a maximum of 0.028 ppm and decreased to nondetectable (<0.01) levels by study day 18. Cream from cows dosed at 40X had pirimiphos-methyl residues of 0.247 and 0.122 ppm on study days 14 and 27, respectively; metabolite R36341 residues in cream were 0.255 and 0.069 ppm on study days 14 and 27, respectively.

No pirimiphos-methyl or metabolite R36341 residues were detected (<0.05 ppm) in muscle (meat) from any dosing level. Metabolite R36341 was not detected (<0.02 ppm) in liver from

any dosing level. In samples from cows dosed at 4X, pirimiphos-methyl residues were <0.02-0.023 ppm in liver and were nondetectable in kidney and fat; metabolite R36341 was detected in kidney and fat at <0.02-0.027 and <0.02-0.023 ppm respectively. At 12X, pirimiphos-methyl residues were <0.02 ppm (nondetectable) in kidney, and ranged from 0.044 to 0.078 ppm in fat; metabolite R36341 residues ranged from 0.029 to 0.072 ppm in kidney and were 0.043 to 0.109 ppm in fat. At 40X, the parent was present at up to 0.029 ppm in kidney and 0.129 ppm in fat; the metabolite R36341 was present in kidney at a maximum of 0.026 ppm and in fat at 0.023 to 0.089 ppm.

Table 5. Pirimiphos-methyl and Metabolite Residues in Milk/Cream.

Dose interval	Residues (ppm) [a]	
	Pirimiphos-methyl	R36341
Milk		
120 ppm day 7	<0.010	<0.010
day 14	<0.010	<0.010
day 21	<0.010	<0.010
day 27	<0.010	<0.010
400 ppm day 1	<0.010	<0.010
day 3	0.024	0.020
day 5	0.034	0.028
day 7	0.026	0.023
day 10	0.014	0.011
day 14	0.017	0.012
day 18	0.012	<0.010
day 21	0.017	0.011
day 24	<0.010	<0.010
day 27	<0.010	<0.010
Cream		
120 ppm day 14	0.044	0.059
day 27	0.028	0.026

Table 5. Pirimiphos-methyl and Metabolite Residues in Milk/Cream.

Dose interval	Residues (ppm) [a]	
	Pirimiphos-methyl	R36341
400 ppm day 14	0.247	0.255
day 27	0.122	0.069

[a] Values are means of samples from 3 cows; residues corrected for concurrent recovery of each analyte.

[b] Non-detectable analytes added as the respective LOQs.

Table 6. Pirimiphos-methyl and Metabolite Residues in Edible Tissues from Cows.

Dose	Residues (ppm) [a]	
	Pirimiphos-methyl	R36341
Liver		
40 ppm	<0.020-0.023	<0.020
120 ppm	0.028-0.039	<0.020
400 ppm	<0.020	<0.020
Kidney		
40 ppm	<0.020	<0.020-0.027
120 ppm	<0.020	0.029-0.072
400 ppm	0.022-0.029	<0.020-0.026
Muscle		
40 ppm	<0.050	<0.050
120 ppm	<0.050	<0.050
400 ppm	<0.050	<0.050
Fat		
40 ppm	<0.020	<0.020-0.022
120 ppm	0.044-0.078	0.043-0.109
400 ppm	0.078-0.129	0.023-0.089

Table 6. Pirimiphos-methyl and Metabolite Residues in Edible Tissues from Cows.

Dose	Residues (ppm) [a]	
	Pirimiphos-methyl	R36341
Skin/fat		
40 ppm	<0.020	<0.020
120 ppm	<0.020-0.041	0.035-0.088
400 ppm	0.048-0.151	0.029-0.067

[a] Ranges represent three samples; residues corrected for concurrent recovery of each analyte.

[b] Total residues are the mean of three cows; non-detectable analytes added as the respective LOQs.

Poultry

For residues in poultry commodities, refer to Tables 7 and 8. Residues of the metabolite R36341 were nondetectable (<0.02 ppm) in eggs, muscle (meat), meat by-products, fat and fat/skin from poultry dosed at 8X and 24X the maximum theoretical dietary burden. At 8X, pirimiphos methyl residues were nondetectable (<0.02 ppm) in eggs. At 24X, the maximum pirimiphos-methyl residue in eggs was 0.033 ppm on day 14.

Pirimiphos-methyl residues were nondetectable (<0.02 ppm) in liver and muscle from hens dosed at 8 and 24X. In fat, parent residues were 0.024 to 0.044 ppm at the 8X dosing level, and 0.097-0.154 at the 24X dosing level. In skin/fat, pirimiphos-methyl residues were <0.02 to 0.021 at the 8X dosing level, and 0.031 to 0.070 at the 24X dosing level.

Table 7. Pirimiphos-methyl and Metabolite Residues in Eggs.

Dose interval	Residues (ppm) [a]	
	Pirimiphos-methyl	R36341
52 ppm day 7	<0.02	<0.02
day 14	<0.02	<0.02
day 21	<0.02	<0.02
day 28	<0.02	<0.02

Table 7. Pirimiphos-methyl and Metabolite Residues in Eggs.

Dose interval	Residues (ppm) [a]	
	Pirimiphos-methyl	R36341
157 ppm day 1	<0.02	<0.02
day 3	<0.02	<0.02
day 5	<0.02	<0.02
day 7	<0.02	<0.02
day 10	<0.02	<0.02
day 14	0.033	<0.02
day 18	<0.02	<0.02
day 21	0.021	<0.02
day 24	<0.02	<0.02
day 28	0.030	<0.02

[a] Values are the mean of 2-4 subgroups of eggs pooled from each dose group and collection day; residues were corrected for concurrent recovery of each analyte.

[b] Non-detectable analytes added as the respective LOQs.

Table 8. Pirimiphos-methyl and Metabolites Residues in Edible Tissues of Hens.

Dose	Residues (ppm) [a]	
	Pirimiphos-methyl	R36341
Liver		
47 ppm	<0.020	<0.020
141 ppm	<0.020	<0.020
Muscle		
47 ppm	<0.020	<0.020
141 ppm	<0.020	<0.020
Fat		

Table 8. Pirimiphos-methyl and Metabolites Residues in Edible Tissues of Hens.

Dose	Residues (ppm) [a]	
	Pirimiphos-methyl	R36341
47 ppm	0.024-0.044	<0.020
141 ppm	0.097-0.154	<0.020
Skin/fat		
47 ppm	<0.02-0.021	<0.020
141 ppm	0.031-0.070	<0.020

[a] Values are the ranges of 2-4 subgroups of each tissue pooled from each dose group; residues were corrected for concurrent recovery of each analyte.

[b] Non-detectable analytes added as the respective LOQs.

Storage Stability Data (MRID Nos. 440646403, 44064604)

Milk, eggs, and tissues from untreated animals supplied by Huntingdon Research Centre were fortified with pirimiphos-methyl and its metabolite R36341. Fortified samples were analyzed on day 0 and after 3 and 6 months in storage at -20 C. The data demonstrate that pirimiphos-methyl *per se* and metabolite R36341 are stable in all livestock matrices stored frozen for up to 6 months. The 6-month storage interval is sufficient to demonstrate stability of pirimiphos-methyl and metabolite residues in livestock matrices during the intervals incurred in livestock feeding studies. The results are presented in Tables 9 and 10.

Table 9. Mean Corrected Percent Recoveries of Pirimiphos-methyl and its Metabolites from Stored Cattle Matrices.

Tissue	Time, weeks (nominal)	Pirimiphos-methyl	R36341
Whole milk	0	81.3	96.5
	0.1	129	100
	12	96.4	104
	30	93.5	107
Cream	0	90.0	88.4
	13	99.8	103
	26	100	94.7

Table 9. Mean Corrected Percent Recoveries of Pirimiphos-methyl and its Metabolites from Stored Cattle Matrices.

Tissue	Time, weeks (nominal)	Pirimiphos-methyl	R36341
Muscle	0	91.5	102
	19	104	77.5
	25	109	78.6
Kidney	0	84.5	91.5
	20	104	87.1
	25	82.0	120
Liver	0	77.5	86.5
	20	87.6	87.0
	26	96.0	105
Skin plus underlying fat	0	97.3	99.0
	19	88.1	105
	26	104	87.9

Table 10. Mean Corrected Percent Recoveries of Pirimiphos-methyl and its Metabolites from Stored Hen Matrices.

Tissue	Time, weeks (nominal)	Pirimiphos-methyl	R36341
Eggs	0	72.3	80.0
	15	98.7	126
	28	101	86.0
Liver	0	108	98.4
	16	95.9	98.4
	25	106	84.7
Muscle	0	101	115
	16	112	77.9
	24	106	94.4
Abdominal fat	0	95.8	102
	16	101	100
	24	93.1	101
Skin plus subcutaneous fat	0	91.8	97.7
	19	103	89.7
	24	97.9	102

Discussion/Conclusions

The ruminant and poultry feeding studies are adequate, and are supported by adequate analytical methods, raw data and storage stability data.

Ruminants

Based on data from the ruminant feeding study, and on the inclusion of only the parent, pirimiphos-methyl, in the tolerance expression, tolerances for residues in meat and milk can be classified under category 3 of 40 CFR §180.6(a), i.e. there is no reasonable expectation of detectable residues. Therefore, tolerances for residues in meat and milk are not necessary, and should be revoked. Tolerances for residues in liver and kidney and in the fat and meat by-products of cattle, goats, hogs, horses and sheep should be revised (decreased) to 0.02 ppm.

Poultry

With the revision of the tolerance definition to include only the parent compound, data from the poultry feeding study indicate that tolerances for residues in eggs, poultry meat and meat by-products can be classified under category 3 of 40 CFR §180.6(a). Therefore, tolerances for residues in eggs, and in poultry meat and meat by-products should be revoked. The tolerance for residues in poultry fat should be revised (decreased) to 0.02 ppm.

The recommended changes in the tolerances for residues in poultry and ruminant commodities should be included in the tolerance reassessment summary for the residue chemistry chapter of the HED RED.

MASTER RECORD IDENTIFICATION NUMBERS

00080777 Plant Protection Limited (19??) Determination of Residues of Pirimiphos-methyl and Its Phosphorus-containing Metabolites in Crops, Water, Milk and Animal Tissues. Undated residue analytical method no. 11A. (Unpublished study received Dec 1, 1978 under 10182-EX-15; submitted by ICI Americas, Inc., Wilmington,Del.; CDL:097674-S).

44046401 Robinson, J. (1996) Pirimiphos-Methyl, R36341, R46382, R35510 and R4039: Validation of the Methods of Analysis for Pirimiphos-Methyl and Its Metabolites in Hen Matrices: Lab Project Number: 94066-WECO: CSL 2/951973. Unpublished study prepared by Huntingdon Research Centre Ltd. 316 p.

44046402 Cameron, D. (1996) Magnitude of Residues of Pirimiphos-Methyl and Its Metabolites in Tissues and Eggs of Laying Hens Fed a Diet Containing Pirimiphos-MProject Number: PRO-R-011-88: Lab Project Number: CSL 6: CSL 6/961568: S5200-005-R. Unpublished study prepared by Huntingdon Research Centre Ltd. 397 p.

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